

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

1. (Currently Amended) A system composition of matter comprising ~~[[: a]]~~ one or more biomolecule and biomolecule in combination with a single metal particle, wherein said single metal particle and at least one of said one or more biomolecule are positioned at a distance apart sufficient to affect adjust intrinsic emission of electromagnetic radiation emission of at least one of said one or more biomolecule from the biomolecule upon exposing said system in response to an amount of exciting electromagnetic radiation.

2. (Currently Amended) The system composition of claim 1, wherein each of the one or more biomolecule comprises a nucleic acid is individually a member selected from the group consisting of a nucleoside, a nucleotide, a purine, a pyrimidine, an oligonucleotide, a polynucleotide, an amino acid, a peptide, a protein, a lipid and a sugar moiety.

3.-9. (Canceled).

10. (Currently Amended) The system composition of claim 1, wherein the single metal particle is at a distance of about 50 Å to about 2000 Å from the biomolecule.

11. (Currently Amended) The system composition of claim 1, wherein the single metal particle comprises a noble metal.

12. (Currently Amended) The system composition of claim 11, wherein the noble metal is selected from the group consisting of rhenium, ruthenium, rhodium, palladium, silver, osmium, iridium, platinum, and gold.

13. (Currently Amended) The system composition of claim 1, wherein the single metal particle is sub-wavelength in size.

14. (Currently Amended) The system composition of claim 1, wherein the one or more biomolecule is linked to the single metal particle.

15.-27. (Canceled).

28. (New) A system comprising a test sample and one or more metal particles arranged on a solid support, wherein said test sample comprises one or more biomolecule, and wherein said one or more metal particles and at least one of said one or more biomolecule in said test sample are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecule upon exposing said system to exciting electromagnetic radiation, and wherein an extrinsic fluorescent marker is not a part of the system.

29. (New) The system of claim 28, wherein said support is glass or quartz.

30. (New) The system of claim 28, wherein said one or more metal particles is multiple metal particles arranged as an array of islands on said support.

31. (New) The system of claim 28, wherein said one or more metal particles is multiple metal particles in the form of a film on said support.

32. (New) The system of claim 28, wherein said one or more metal particles is coated with a polymer, a gel, an adhesive, an oxide or a biological material.

33. (New) The system of claim 28, wherein said one or more metal particles is coated with an oxide.

34. (New) The system of claim 28, wherein one or more second biomolecule is attached to said one or more metal particles, and intrinsic emission of electromagnetic radiation of at least one of said one or more second biomolecule is affected upon exposing said system to exciting electromagnetic radiation.

35. (New) The system of claim 33, wherein one or more second biomolecule is attached to said one or more metal particles, and intrinsic emission of electromagnetic radiation of at least one of said one or more second biomolecule is affected upon exposing said system to exciting electromagnetic radiation.

36. (New) The system of claim 28, 34 or 35, wherein each biomolecule of said one or more biomolecule and each biomolecule of said one or more second biomolecule is individually a member selected from the group consisting of a nucleoside, a nucleotide, a purine, a pyrimidine, an oligonucleotide, a polynucleotide, an amino acid, a peptide, a protein, a lipid and a sugar moiety.

37. (New) The system of claim 28, wherein said one or more metal particles comprises a noble metal.

38. (New) The system of claim 37, wherein said noble metal is a member selected from the group consisting of rhenium, ruthenium, rhodium, palladium, silver, osmium, iridium, platinum and gold.

39. (New) The system of claim 30, wherein each of said one or more metal particles is sub-wavelength in size.

40. (New) The system of claim 28, wherein the surface of each of said one or more metal particles is at a distance of about 50 Å to about 2000 Å from the biomolecule.

41. (New) The system of claim 28, 34 or 35, wherein said affect on intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecule or at least one of said one or more second biomolecule is an enhancement of intrinsic emission.

42. (New) The system of claim 28, wherein said electromagnetic radiation has a wavelength of from about 280 nm to about 295 nm.

43. (New) The system of claim 28, wherein said electromagnetic radiation has a wavelength of about 520 nm.

44. (New) The system of claim 34 or 35, wherein said intrinsic emission of electromagnetic radiation of at least one of said one or more second biomolecule is affected in response to binding by a biomolecule in said test sample.

45. (New) The system of claim 28, 34 or 35, wherein said exciting electromagnetic radiation is multi-photon excitation.

46. (New) A system comprising a test sample and a suspension of one or more metal particles, wherein said test sample comprises one or more biomolecule, and wherein one or more metal particles and at least one of said one or more biomolecule in said sample are positioned at a distance apart sufficient to affect electromagnetic radiation emission of at least one of said one or more biomolecule upon exposing said system to exciting electromagnetic radiation.

47. (New) The system of claim 46, wherein said suspension of one or more metal particles is a colloidal suspension.

48. (New) The system of claim 46, wherein said one or more metal particles is coated with a polymer, a gel, an adhesive, an oxide or a biological material.

49. (New) The system of claim 46, wherein said one or more metal particles is coated with an oxide.

50. (New) The system of claim 46, wherein each of said one or more metal particles is sub-wavelength in size.

51. (New) The system of claim 46, wherein the surface of each of said one or more metal particles is at a distance of about 50 Å to about 2000 Å from the biomolecule.

52. (New) The system of claim 46 or 48, wherein one or more second biomolecule is attached to said one or more metal particles, and electromagnetic radiation emission of at least one of said one or more second biomolecule is affected upon exposing said system exciting electromagnetic radiation.

53. (New) The system of claim 46, wherein said one or more biomolecule is labeled with an extrinsic fluorescent marker.

54. (New) The system of claim 52, wherein said one or more second biomolecule is labeled with an extrinsic fluorescent marker.

55. (New) The system of claim 53, wherein said extrinsic fluorescent marker is a fluorophore.

56. (New) The system of claim 54, wherein said extrinsic fluorescent marker is a fluorophore.

57. (New) The system of claim 52, wherein said electromagnetic radiation emission of at least one of said one or more second biomolecule is affected in response to binding by a biomolecule in said test sample.

58. (New) The system of claim 46, wherein each of said one or more biomolecule is individually a member selected from the group consisting of a nucleoside, a nucleotide, a purine, a pyrimidine, an oligonucleotide, a polynucleotide, an amino acid, a peptide, a protein, a lipid and a sugar moiety.

59. (New) The system of claim 52, wherein each of said one or more second biomolecule is individually a member selected from the group consisting of a nucleoside, a nucleotide, a purine, a pyrimidine, an oligonucleotide, a polynucleotide, an amino acid, a peptide, a protein, a lipid and a sugar moiety.

60. (New) The system of claim 46, wherein said one or more metal particles comprises a noble metal.

61. (New) The system of claim 60, wherein said noble metal is selected from the group consisting of rhenium, ruthenium, rhodium, palladium, silver, osmium, iridium, platinum, and gold.

62. (New) The system of claim 46, wherein said affect on electromagnetic radiation emission of at least one of said one or more biomolecule is an enhancement of emission.

63. (New) The system of claim 52, wherein said affect on electromagnetic radiation emission of at least one of said one or more second biomolecule is an enhancement of emission.

64. (New) The system of claim 46, wherein said electromagnetic radiation has a wavelength of from about 280 nm to about 295 nm.

65. (New) The system of claim 46, wherein said electromagnetic radiation has a wavelength of about 520 nm.

66. (New) The system of claim 46 or 55, wherein said exciting electromagnetic radiation is multi-photon excitation.

67. (New) A composition comprising a metal particle coated with one or more biomolecule, wherein said metal particle and at least one of said one or more biomolecule are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecule upon exposing said metal particle to exciting electromagnetic radiation, and wherein an extrinsic fluorescent marker is not a part of said composition.

68. (New) The composition of claim 67, wherein said one or more biomolecule is a member selected from the group consisting of a nucleoside, a nucleotide, a purine, a pyrimidine, an oligonucleotide, a polynucleotide, an amino acid, a peptide, a protein, a lipid and a sugar moiety.

69. (New) The composition of claim 67, wherein said metal particle comprises a noble metal.

70. (New) The composition of claim 69, wherein said noble metal is selected from the group consisting of rhenium, ruthenium, rhodium, palladium, silver, osmium, iridium, platinum, and gold.

71. (New) The composition of claim 67, wherein each of said metal particle is sub-wavelength in size.

72. (New) The composition of claim 67, wherein said distance between the surface of each of said metal particles and said one or more biomolecules is about 50 Å to about 2000 Å.

73. (New) The composition of claim 67, wherein said composition is a suspension of one or more of said metal particle coated with one or more biomolecule.

74. (New) The composition of claim 73, wherein said suspension is a colloidal suspension.

75. (New) The composition of claim 67, wherein said metal particle is coated with an intermediate layer between said metal particle and said one or more biomolecule, wherein said intermediate layer is a member selected from the group consisting of a polymer, a gel, an adhesive, and an oxide.

76. (New) The composition of claim 75, wherein said intermediate layer is an oxide.

77. (New) The composition of claim 67, wherein said affect on intrinsic emission of electromagnetic radiation is an enhancement of intrinsic emission.

78. (New) The composition of claim 67, wherein said electromagnetic radiation has a wavelength of about 280 nm to about 295 nm.

79. (New) The composition of claim 67, wherein said electromagnetic radiation has a wavelength of about 520 nm.

80. (New) The composition of claim 67, wherein said one or more biomolecule may be the same or different.

81. (New) The composition of claim 67, wherein said electromagnetic radiation emission of said one or more biomolecule is affected by a biomolecule in a test sample.

82. (New) The composition of claim 67, wherein said exciting electromagnetic radiation is multi-photon excitation.



**REMARKS**

Claims 1-27 are pending; claims 15-25 have been withdrawn from consideration; claims 1-14 and 26-27 are rejected.

The present Amendment directs the cancellation of non-elected claims 15-25, and claims 3-9 and 26-27.

The present Amendment directs the addition of new claims 28-82.

After entry of this amendment, claims 1-2, 10-14 and 28-82 will be pending.

Claim 1 now recites a system comprising one or more biomolecules and a single metal particle. Support for the use of a single metal particle may be found through the specification, such as at page 3, lines 17-19, where such a system is specifically disclosed.

Amended claim 2 combines the elements of claims 2-9.

New claims 28-45 recite a system comprising a test sample and one or more metal particles arranged on a solid support, “wherein an extrinsic fluorescent marker is not a part of the system.” Support for such a system lacking an extrinsic fluorescent marker may be found throughout the specification, for example at page 12, lines 13-16.

New claims 46-66 recite a system comprising a test sample and a suspension of one or more metal particles. Support for the use of a suspension of one or more metal particles may be found in the specification, for example at page 13, lines 9-10.

New claims 67-82 recite a composition comprising a metal particle coated with one or more biomolecules, “wherein an extrinsic fluorescent marker is not a part of said composition.” Support for the use of a metal particle coated with the biomolecules may be found in the

specification, for example at page 13, lines 19-21, and at page 24, line 27, through page 25, line 5.

No new matter has been added. Entry of the Amendment is respectfully requested.

**I. Formal Matters**

A. Applicants thank the Examiner for providing a signed and initialed copy of the lists of references, included with the three Information Disclosure Statements (IDS) submitted in this application, with the Office Action date March 27, 2003.

However, the copy of the list submitted with the first IDS (on February 11, 2002), was not complete as only pages 1 and 3 of this list were received by Applicants. Applicants respectfully request the Examiner to provide Applicants with an acknowledged copy of the missing page with the next paper issued by the Patent Office. For the Examiner's convenience, a copy of the missing page is enclosed herewith.

B. Applicants note that the Examiner has not yet acknowledged Applicant's claim for domestic priority to U.S. provisional application number 60/268,326, filed February 14, 2001. Applicants respectfully request such acknowledgement be made in the next paper issued by the Patent Office.

**II. Restriction/Election**

At paragraphs 1-3 of the Office Action, the Examiner sets forth in writing the Restriction Requirement issued in this application on January 28, 2003. The Examiner further states that Applicants provisionally elected Group I, claims 1-14 and 26-27, without traverse. The Examiner requires affirmation of the election.

Applicants hereby affirm the election of Group I, claims 1-14 and 26-27. Included herewith is an amendment to the claims, canceling non-elected claims 15-25. Applicants reserve the right to file the non-elected claims in a divisional application.

### **III. Rejection of Claims Under 35 U.S.C. §102**

At paragraph 6 of the Office Action, claims 1-14 and 26-27 are rejected under 35 U.S.C. §102(b) as being anticipated by Schalkhammer et al. (USP 5,866,433, issued February 2, 1999).

In general, the Examiner states that Schalkhammer et al. teaches a composition of matter comprising a biomolecule in combination with a metal particle, wherein the metal particle and the biomolecule are positioned at a distance apart sufficient to adjust intrinsic emission of electromagnetic radiation from the biomolecule in response to an amount of exciting electromagnetic radiation, as is recited in claim 1 of the pending application.

In response, Applicants note that included herewith is an amendment revising the pending claims and adding a number of new claims. Applicants assert that the subject matter recited in the amended claims, and in the new claims, is not anticipated by the disclosure of Schalkhammer et al.

#### Pending claims 1-2 and 10-14

With regard to pending claims 1-2 and 10-14, these claims are directed to a system comprising one or more biomolecules in combination with a “single” metal particle. In contrast, a close reading of Schalkhammer et al. reveals that the sensor taught therein makes use of multiple metal particles in every embodiment of the sensor.

As Schalkhammer et al. does not teach or suggest a sensor using only one metal particle, as recited in claims 1-2 and 10-14 of the present application, Schalkhammer et al. does not anticipate the cited claims and Applicants respectfully request reconsideration and withdrawal of this rejection.

New claims 28-45

With regard to new claims 28-45, these claims recite a system comprising a test sample and one or more metal particles arranged on a solid support, “wherein an extrinsic fluorescent marker is not a part of the system.” Thus, these new claims encompass a system that does not include an extrinsic fluorescent marker. In contrast, in each embodiment of the system of Schalkhammer et al., an extrinsic fluorescent marker is used. Thus, while the system of the present application relies on the detection of only intrinsic emission of electromagnetic radiation, the system of Schalkhammer et al. requires the addition of a supplemental fluorescent marker and detection of both intrinsic and extensive emission of electromagnetic radiation.

As the system recited in new claims 28-45 does not require an extrinsic fluorescent marker, and the sensor of Schalkhammer et al. does, these new claims are not taught or suggested by the disclosure of Schalkhammer et al.

New claims 46-66

With regard to new claims 46-66, these claims recite a system comprising a test sample and a suspension of one or more metal particles. As Schalkhammer et al. does not teach or suggest the use of a suspension of one or more metal particles (all embodiments use a support on which metal islands are deposited), the cited reference does not anticipate or make obvious the subject matter recited in these new claims.

New claims 67-82

With regard to new claims 67-82, these claims recite a composition comprising a metal particle coated with one or more biomolecules, “wherein an extrinsic fluorescent marker is not a part of said composition.” As discussed above with regard to claims 28-45, the metal particles recited in these claims specifically exclude an extrinsic fluorescent marker. In contrast, in each embodiment of the system taught by Schalkhammer et al., the use of a fluorophore is required. Thus, Schalkhammer et al. relies on the use of extrinsic fluorescence produced by the fluorophore. In contrast, as recited in the new claims, the Applicants’ metal particles specifically disclaim the use of an extrinsic fluorophore. Instead, Applicants’ system is based on measuring the intrinsic fluorescence emitted by the biomolecule itself.

As Schalkhammer et al. does not teach or suggest the use of a metal particle without an extrinsic fluorescent marker, this patent does not anticipate or make obvious the subject matter recited in these new claims.

**IV. Conclusion**


In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

AMENDMENT UNDER 37 C.F.R. §1.111  
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The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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